Superselective Arterial Chemotherapy for Inoperable Metastases in the Dura Mater and Cranium

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Summary

Diffuse metastases to the cranium and dura mater of the bilateral hemisphere do not allow surgical intervention. We describe an excellent case which was treated by intra-arterial chemotherapy using Epirubicine (Farumorbicine).

A 58-year-old woman treated for breast cancer ten years ago was admitted to our hospital with headache and frontal mass lesions. Magnetic resonance (MR) imaging on admission revealed a remarkable enhanced lesion of the bilateral dura mater and cranium, and bilateral brain edema in the frontal lobe. Angiography disclosed a vascular rich tumour supplied by bilateral external carotid artery branches. We successfully treated the lesion using superselective intra-arterial chemotherapy with a minimal dose of Epirubicine followed by embolization of bilateral external carotid artery branches. Follow-up MR imaging two years after the endovascular treatment showed disappearance of the enhanced lesion and remodeling of the skull bone. The patient is neurologically free of symptoms.

Introduction

In 1904, Dawbarn et Al [1] firstly reported a craniocervical malignant tumour fed by external carotid artery branches embolized with paraffin and waserin via an intra-arterial route.

Thereafter, intra-arterial chemotherapy using nitrogen mustard was reported by Klopp et Al [2] for intracranial epidermoid cancer. For the patients with liver or renal cancer, the same basic approach is widely used as a conventional treatment [3]. On the other hand, endovascular intervention is generally the only a therapeutic option for brain neoplasms. The purpose is mainly to diminish bleeding during surgery for vascular rich tumours as a preoperative procedure. Here case of inoperable diffuse metastatic tumour is presented, successfully treated with intra-arterial chemotherapy.

Case Report

A 58-year-old woman with a history of breast cancer for which she had been treated ten years previously, was admitted to our hospital suffering from headache for three months and frontal mass.

Skull X-rays showed osteolytic lesions over the whole skull except the temporal bone (figure 1). Computed tomography (CT) scan demonstrated enhanced lesions located in the dura mater beyond these and associated brain edema in the bilateral frontal lobe (figure 2). Magnetic resonance (MR) imaging revealed remarkable brain edema around the enhanced lesions (figure 3) and angiography showed a vascular rich tumour supplied by the external carotid artery branches in the bilateral dura

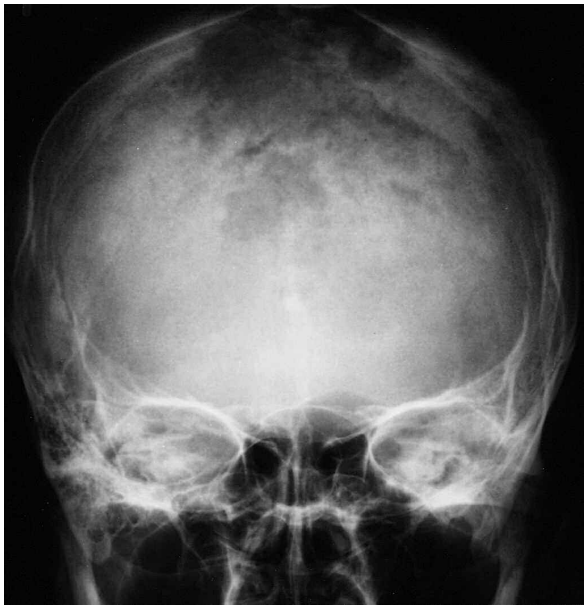


Figure 1 Plain skull roentgenogram showing erosion of the skull.

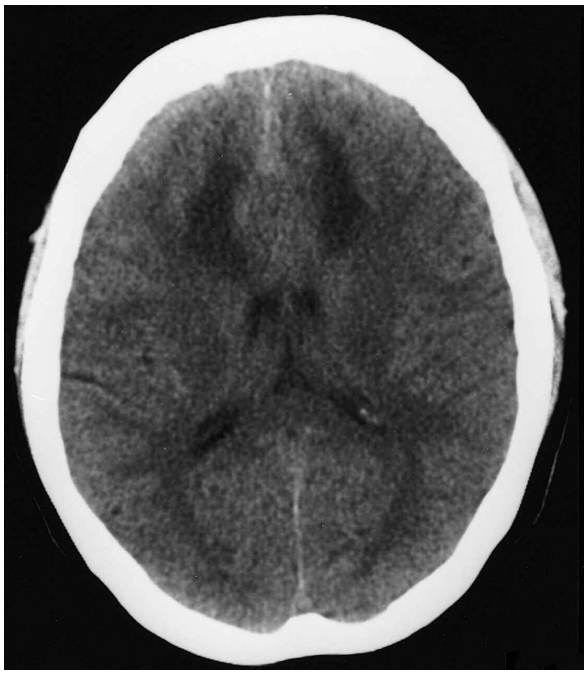
mater and cranium (figure 4). Galium scintigrams showed no recurrence of primary lesions or metastases other than these cranial lesions. After receipt of informed consent, intra-arterial chemotherapy via external carotid branches was performed.

Initially the right superficial temporal artery (STA) and middle meningeal artery (MMA) were superselectively catheterized and each infused slowly with 5 mg of Epirubicin (Farumorbicin) diluted in 10 ml of contrast medium followed by obliteration with platinum particles ranging from 150-250 microns in size. Next, the left STA, MMA and accessory meningeal artery (AMA) were each injected with 3 mg of Epirubicin diluted in 6 ml of contrast medium followed again by embolization. At 14 days after the firstangiogram, follow up angiography showed that the bilateral MMA and right STA were partially recanalized, and second intra-arterial chemotherapy and embolization were performed.

For this, the right MMA and STA were each infused with 5 mg of Epirubicin diluted in 10 ml of contrast medium followed by embolization with platinum particles. The left MMA was also infused with 10 mg of Epirubicin diluted in 20 ml of contrast medium followed by embolization. The total dose of Epirubicin was 39 mg.

After endovascular treatment, the patient's clinical course was uneventful. Eruptions on the scalp were recognized but mild and had disappeared completely after one month. Hormone therapy using medroxyprogesterone ac-

A



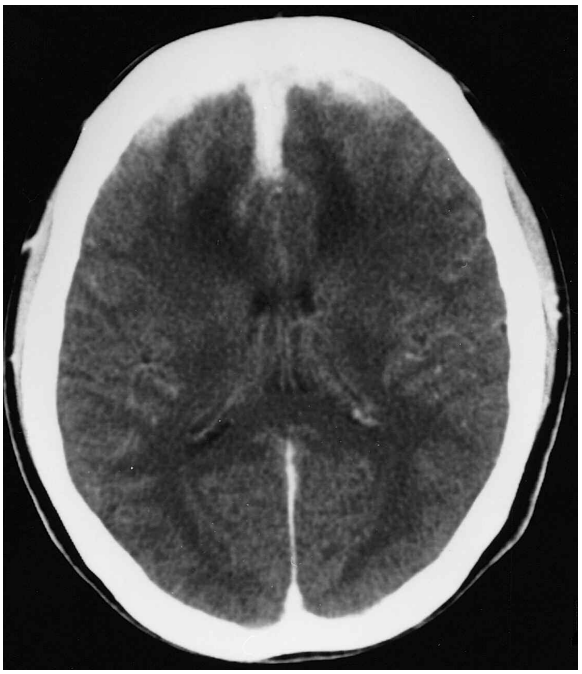


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Figure 2 Plain (A) and enhanced (B) computed tomography (CT) scans showing a tumor limited to the cranium and dura.

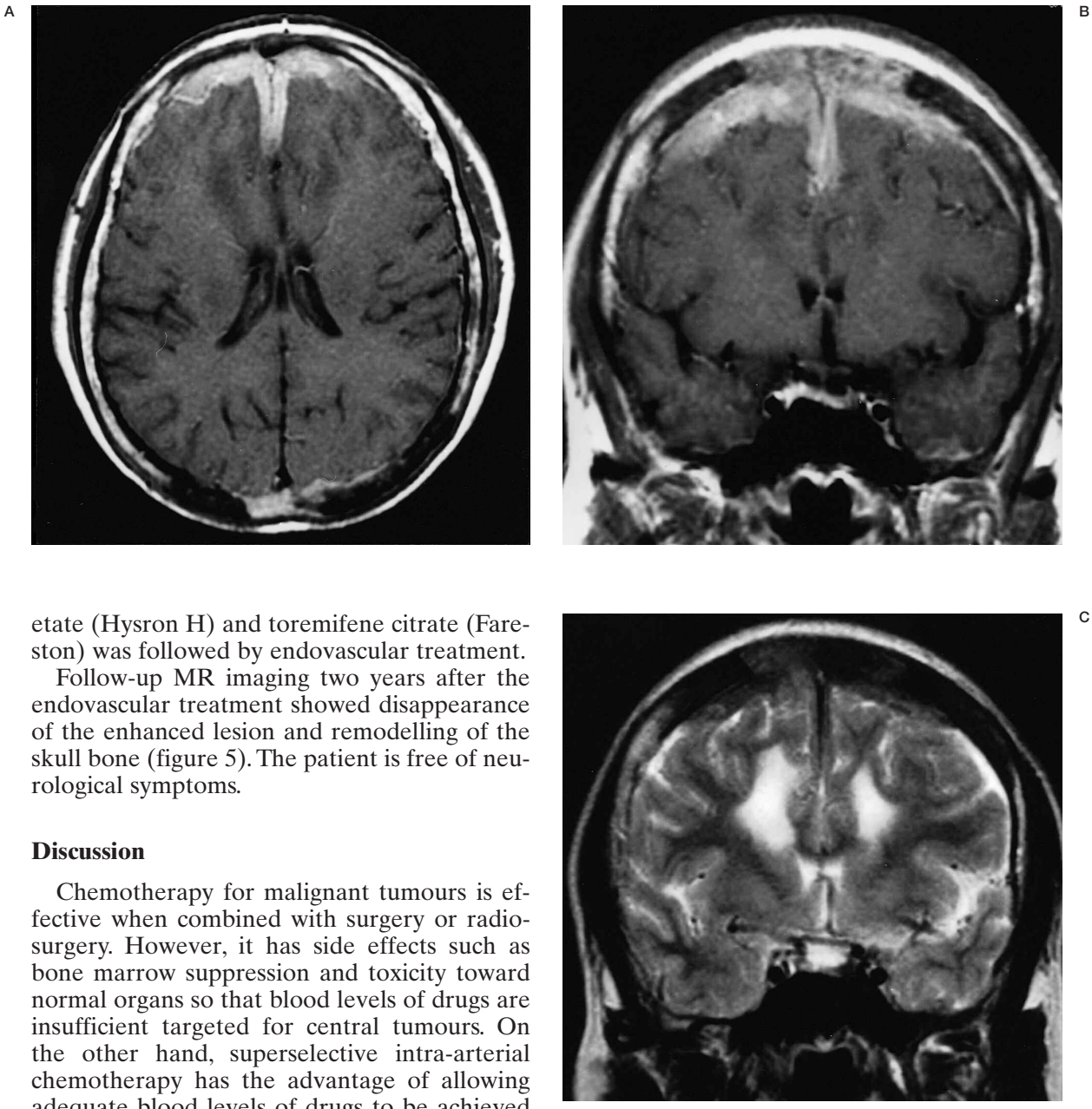

Figure 3 MR imaging T1-weighted axial (A) and coronal image (B) after contrast injection, and T2-weighted coronal images (C) showing abnormalities of the cranium and dura with marked brain edema.

etate (Hysron H) and toremifene citrate (Fareston) was followed by endovascular treatment.

Follow-up MR imaging two years after the endovascular treatment showed disappearance of the enhanced lesion and remodelling of the skull bone (figure 5). The patient is free of neurological symptoms.

Discussion

Chemotherapy for malignant tumours is effective when combined with surgery or radiosurgery. However, it has side effects such as bone marrow suppression and toxicity toward normal organs so that blood levels of drugs are insufficient targeted for central tumours. On the other hand, superselective intra-arterial chemotherapy has the advantage of allowing adequate blood levels of drugs to be achieved in local vascular beds of the targeted tumour. In fact, for liver and renal cancers, superselective intra-arterial chemotherapy has become a conventional treatment. However, for intracranial lesions, even if intra-arterial chemotherapy is performed superselectively, it is generally avoided because of the danger of damaging the optic nerve and leucoencephalopathy [4]. With malignant brain tumours, intra-arterial chemotherapy is ruled out by such dominant side effects outweighing the advantages.

Several reports of intra-arterial chemotherapy for intracranial malignant tumours have been published, but these were limited to patients with malignant gliomas [5]. ACNU, BCNU, cisplatin and carboplatin were applied for this superselective arterial chemotherapy, at total doses of 100-130 mg, 100 mg, 286 mg and 60 mg/m^2, respectively [5,6,7].

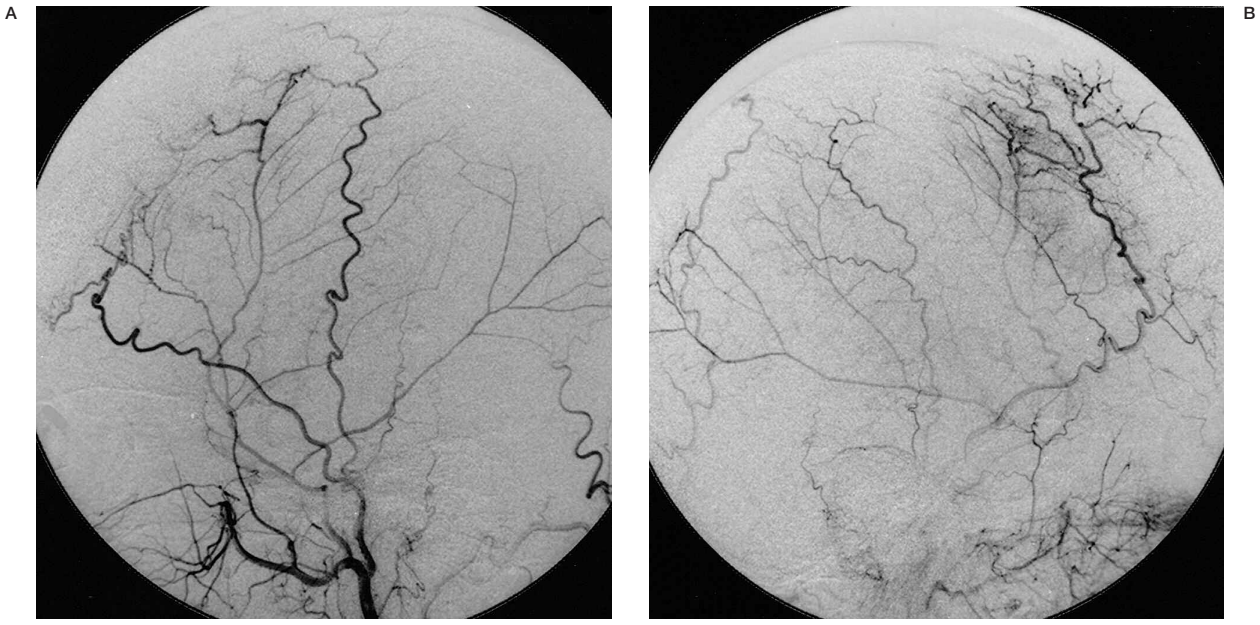

Figure 4 Preembolization lateral left (A) and right (B) external carotid artery angiograms demonstrating tumor staining from MMA, STA and OA.

Brain metastasis from breast cancer is reported to account for 15% of all metastatic brain tumours in Japan [8]. There is a particular tendency to metastasise to the dura mater and skull.

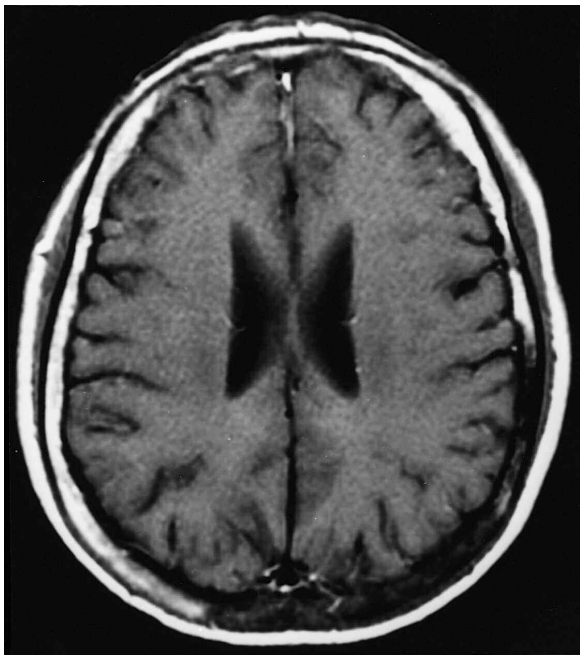

Figure 5 Follow up MR imaging 12 months after embolization showing. A disappearance of abnormalities of the cranium and dura.

When metastases to the brain or and other organs are recognized, the median survival is reported to be about one year with only 25% surviving for two years [9]. With such a poor prognosis, aggressive treatments may be inappropriate.

On the other hand, metastases from breast cancer may show a positive response to treatment resulting in good outcome. Chemotherapy for metastatic brain tumours from breast cancer has been performed using cyclophosphamide, 5-fluorpuracil, methothorexiate, vincristin, and adriamycine, alone or in combination [10]. Recently, Epirubicine (Farmorbicine) has become available with or without other drugs followed by hormone therapy using medroxyprogesterone [11-13].

In the present case, Epirubicine was employed for chemotherapy followed by hormone therapy and this resulted in a good outcome. Epirubicine belongs to the anti-tetracyclinic group of drugs with antibiotic and anticancer effects, acting on the DNA and RNA of tumour cells.

Since 1995, Epirubicine has been available in Japan for breast and liver cancers intravenously, and for bladder cancer intrathecally. Serious side effects have been reported including myocardial dysfunction and bone marrow suppression, especially using more than a total dose of 200 mg.

Intra-arterial chemotherapy with Epirubicin has been documented for a malignant thoracic tumour through the internal thoracic and subclavian arteries [14]. Epirubicine is less toxic for cardial function than adriamycine. Following these reports, Epirubicin is effective for breast cancer, and was using safely for intra-arterial chemotherapy in a past report. In this case, we used pure Epirubicin for intra-arterial chemotherapy. However, intracranial infusion of Epirubicin has to our knowledge never been reported previously and appropriate dosing thus remains to be determined. In this report, the total dose of Epirubicine was 39 mg, less than half a maximum intravenous dose of 60 mg / m^2.

Serious side effects were not encountered with problems limited to skin eruptions around the superficial temporal artery for one month. This suggests that the drug remained for a comparatively long time. This may be due to the embolization after chemotherapy.

However, the complete disappearance of tumour staining evident immediately after the first chemotherapy was followed by reopening, hopefully due to vasospasm produced by Epirubicine.

To prevent vasospasm, dilution of the concentrated drug may be needed.

However, from our results we conclude that for patients with intracranial metastases sensitive to chemotherapy, superselective intra-arterial chemotherapy followed by embolization may be useful to achieve a good outcome, especially in cases with inoperable and vascular rich tumours fed by external carotid arteries.

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